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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: STEM CELL EXPANSION FACTOR BLOCKING A GENE LIMITING HOX-INDUCED EXPANSION AND METHOD THEREOF

(57) Abstract: The present invention relates to a stem cell expansion factor comprising a blocker which reduces expression level of at least one gene normally limiting HOX-induced expansion of stem cells, whereby reducing expression level of said gene enhances expansion of stem cells containing a HOX peptide. The present invention also relates to a composition for enhancing expansion of stem cells comprising an amino acid sequence having the activity of a HOX peptide, wherein said peptide being able to cross a cell membrane, and a blocker which reduces expression level of at least one gene normally limiting HOX-induced expansion of stem cells, whereby reducing expression level of said gene in the presence of a HOX peptide enhances expansion of stem cells. The preferred HOX peptide is HOXB4 and the preferred gene is PBX.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C07K14/47 A61K38/17 A61K31/7088

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EMBASE, EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BESLU, N. ET AL: "PBX1 is negative regulator of HoxB4-induced Stem Cell Proliferation" BLOOD, vol. 98, no. 11, 16 November 2001 (2001-11-16), pages 451a-452a, XP002275831 43th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 7-11, 2001 Abstract#1891 abstract --- -/--	1-40

☒ Further documents are listed in the continuation of box C.☐ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International Application No

T/CA 03/01539

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BUSKE CHRISTIAN ET AL: "Deregulated expression of HOXB4 enhances the primitive growth activity of human hematopoietic cells" BLOOD, vol. 100, no. 3, 1 August 2002 (2002-08-01), pages 862-868, XP002275832 ISSN: 0006-4971 page 867, paragraph 3</p>	1-40
A	<p>SAUVAGEAU G ET AL: "OVEREXPRESSION OF HOXB4 IN HEMATOPOIETIC CELLS CAUSES THE SELECTIVE EXPANSION OF MORE PRIMITIVE POPULATIONS IN VITRO AND IN VIVO" GENES AND DEVELOPMENT, COLD SPRING HARBOR, NY, US, vol. 9, no. 14, 1995, pages 1753-1765, XP009005048 ISSN: 0890-9369 cited in the application the whole document</p>	
A	<p>ANTONCHUK JENNIFER ET AL: "HOXB4-induced expansion of adult hematopoietic stem cells ex vivo" CELL, vol. 109, no. 1, 5 April 2002 (2002-04-05), pages 39-45, XP002275833 ISSN: 0092-8674 cited in the application the whole document</p>	
A	<p>ANTONCHUK JENNIFER ET AL: "HOXB4 overexpression mediates very rapid stem cell regeneration and competitive hematopoietic repopulation" EXPERIMENTAL HEMATOLOGY (CHARLOTTESVILLE), vol. 29, no. 9, September 2001 (2001-09), pages 1125-1134, XP002275834 ISSN: 0301-472X cited in the application the whole document</p>	

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>THORSTEINSDOTTIR UNNUR ET AL: "Enhanced in vivo regenerative potential of HOXB4-transduced hematopoietic stem cells with regulation of their pool size" BLOOD, vol. 94, no. 8, 15 October 1999 (1999-10-15), pages 2605-2612, XP002275835 ISSN: 0006-4971 cited in the application the whole document</p>	
A	<p>DIMARTINO JORGE F ET AL: "The Hox cofactor and proto-oncogene Pbx1 is required for maintenance of definitive hematopoiesis in the fetal liver" BLOOD, vol. 98, no. 3, 1 August 2001 (2001-08-01), pages 618-626, XP002275836 ISSN: 0006-4971 cited in the application the whole document</p>	
A	<p>SHEN WEI-FANG ET AL: "Hox homeodomain protein exhibit selective complex stabilities with Pbx and DNA" NUCLEIC ACIDS RESEARCH, vol. 24, no. 5, 1996, pages 898-906, XP002275837 ISSN: 0305-1048 the whole document</p>	
A	<p>KROSL JANA ET AL: "Cellular proliferation and transformation induced by HOXB4 and HOXB3 proteins involves cooperation with PBX1" ONCOGENE, vol. 16, no. 26, 2 July 1998 (1998-07-02), pages 3403-3412, XP002275838 ISSN: 0950-9232 the whole document</p>	
P,X	<p>KROSL JANA ET AL: "PBX1 Suppresses the Hematopoietic Stem Cell Growth-Enhancing Effect of HOXB4." BLOOD, vol. 100, no. 11, 16 November 2002 (2002-11-16), page Abstract No. 1128 XP002275839 44th Annual Meeting of the American Society of Hematology; Philadelphia, PA, USA; December 06-10, 2002 ISSN: 0006-4971 abstract</p>	1-40

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INTERNATIONAL SEARCH REPORT

International Application No

ST/CA 03/01539

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>KROSL JANA ET AL: "The competitive nature of HOXB4-transduced HSC is limited by PBX1: The generation of ultra-competitive stem cells retaining full differentiation potential."</p> <p>IMMUNITY, vol. 18, no. 4, April 2003 (2003-04), pages 561-571, XP002275840 ISSN: 1074-7613 (ISSN print) the whole document</p> <p>-----</p>	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 03/01539

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 31-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-3, 6-8, 15-21, 24-28 and 31-40 relate to a compound defined by reference to a desirable characteristic or property, namely its ability to block a gene normally limiting HOX-induced expansion of stem cells, whereby reducing expression level of said gene enhances expansion of stem cells containing a HOX peptide.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds: antisense, nucleic acid, peptide and siRNA.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.